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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,996	04/20/2005	Yongren Benjamin Peng	58768.000007	8890

21967 7590 07/15/2010

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EXAMINER	
PERREIRA, MELISSA JEAN	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
07/15/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/531,996	Applicant(s) PENG ET AL.	
	Examiner MELISSA PERREIRA	Art Unit 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,36 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20,36 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-20,36 and 37 are pending in the application. Claim 37 was newly added in the amendment filed 6/17/10. Any objections and/or rejections from previous office actions that have not been reiterated in this office action are obviated.

New Grounds of Rejection Necessitated by the Amendment

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 37 recites the limitation "the method of claim 36" wherein claim 36 is not drawn to a method claim. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-5,8,10-16,18-20,36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glajch et al. (US 6,455,024 B1) in view of Brow et al. (J. Non-Crystalline Solids 1990, 120, 172-177) and Yashchishin et al. (Glass and Ceramics 1997, 54, 6-8) and in further view of Day et al. (US 5,011,797).

5. Claims 1-5,8-11,13-16,18-20,36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glajch et al. (US 6,455,024 B1) in view of Brow et al. (J. Non-Crystalline Solids 1990, 120, 172-177) and Yashchishin et al. (Glass and Ceramics 1997, 54, 6-8) and in further view of Gilchrist et al. (US 6,143,318).

6. Claims 1-8,10-20,36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glajch et al. (US 6,455,024 B1) in view of Brow et al. (J. Non-Crystalline Solids 1990, 120, 172-177) and Yashchishin et al. (Glass and Ceramics 1997, 54, 6-8) and in further view of Wong et al. (US2004/0131543A1).

7. The rejections stated in the office action mailed 4/16/10 are maintained as stated previously but modified to include newly added claim 37.

8. The nitrogen layer on the surface of the phosphate glass of the combined references of Glajch et al. Brow et al. and/or Yashchishin et al. used to improve it's chemical stability (by 3 to 6 times), mechanical strength, etc. without changing its chemical composition encompasses the nitrogen rich surface layer of the instant claims and is capable of the same functions and has the same properties, such as substantially preventing premature release of said radioactive isotope or combination of radioisotopes for up to 10 half-lives of the longest lived radioisotope in said implant.

Response to Arguments

9. Applicant's arguments filed 6/17/10 have been fully considered but they are not persuasive.

10. Applicant asserts that there is no reason to add a nitrogen surface layer to Glajch’s already nitrided composition. There is no reason why one of skill in the art would modify Glajch’s already nitrided composition by adding more nitrogen- in the form of a nitrogen-rich surface layer, the surface layer being of greater durability than the base glass matrix. Moreover, if a phosphate glass is already nitrided through melting in ammonia (i.e., Glajch's method), there is no reason to have additional surface nitriding since melting is generally done at a much higher temperature than surface nitriding and thus is likely to achieve a much higher nitrogen content as compared to surface nitriding (see discussion below). As such, there is no obvious benefit to include an additional nitriding step. Accordingly, there is no reason to combine Brow's and/or Yashchishin's teachings with Glajch's teachings.

11. The references of Brow's and/or Yashchishin's were not used to teach of modify Glajch’s already nitrided composition by adding more nitrogen- in the form of a nitrogen-rich surface layer but was used to teach of substituting the nitrogen layer of Brow and/or Yashchishin for the nitration of Glajch as the simple substitution of one known, equivalent element for another yields predictable results, such as improved chemical durability and decreased aqueous dissolution rates (Brow) wherein just a few weight percent of nitrogen will suffice to bring about a marked improvement in the properties of a glass, such as the chemical stability (by 3 to 6 times), mechanical strength, etc. (Yashchishin).

12. Applicant asserts that Glajch's base glass has a peak crystallization temperature (T_c) of 360°C and crystallization range from 320°C to 400°C. Brow suggests nitriding

glass near the glass transition temperature (T_g = 345°C), which is close to the peak crystallization temperature (360°C) and within the crystallization range (320°C to 400°C). Therefore, if one of skill in the art applied Brow's methods to Glajch, which they would not, this hypothetical method would likely prepare a crystallized glass-- glass that the instant invention sought to avoid. As such, one of skill in the art would be discouraged from combining Brow with Glajch to attempt to arrive at the claimed implant materials.

13. First, the instant claims are not drawn to the method of making the resorbable implant material and do not exclude crystallized glass.

14. The reference of Brow et al. teaches that most of the glass samples were nitrided at temperatures near the glass transition temperature wherein sodium-barium phosphate glass has a T_g of 354°C. The glass of Glajch et al. (Reidmeyer et al.) teaches that the T_g of $NaPO_3$ is 280°C. Brow et al. further teaches that the glass samples were nitrided at temperatures between 200°C and 425°C for time from 7 to 100 h (p173, left column paragraph 3). Therefore, it would have been obvious to one ordinarily skilled in the art that the nitriding temperature is varied according to the glass sample, so that it is near the T_g, such as near 280°C for $NaPO_3$.

15. Yashchishin teaches that the nitrogen layering of phosphate glass is from 400 to 500°C but the optimum temperature for surface nitriding lies in the interval where the glass can be isothermally held for many hours without being deformed.

16. Therefore, it would have been obvious to one ordinarily skilled in the art that the nitriding temperature is varied according to the glass sample, so that it is near the T_g,

such as near 280°C for $NaPO_3$ or at the optimum temperature where the glass is not deformed.

17. Applicant asserts that Glajch's base glass has a softening temperature (T_s) of 262°C. Brow and Yashchishin perform surface nitriding near glass transition temperature (T_g) and below T_g, respectively. Specifically, Brow suggests nitriding phosphate glasses at 345°C and Yashchishin nitrides phosphate glasses at 400-500°C. As such, if one of skill in the art applied Brow's or Yashchishin's methods to Glajch, which they would not, these hypothetical methods would likely fuse or sinter Glajch's powder into a solid block-glass that the instant invention sought to avoid-because Brow's and Yashchishin's nitriding temperatures are much higher than that softening temperature of Glajch's base glass.

18. The reference of Brow et al. teaches that most of the glass samples were nitrided at temperatures near the glass transition temperature wherein sodium-barium phosphate glass has a T_g of 354°C. The glass of Glajch et al. (Reidmeyer et al.) teaches that the T_g of $NaPO_3$ is 280°C. Brow et al. further teaches that the glass samples were nitrided at temperatures between 200°C and 425°C for time from 7 to 100 h (p173, left column paragraph 3).

19. Yashchishin teaches that the nitrogen doping of phosphate glass is from 400 to 500°C but the optimum temperature for surface nitrogen doping lies in the interval where the glass can be isothermally held for many hours without being deformed.

20. Therefore, it would have been obvious to one ordinarily skilled in the art that the nitriding temperature is varied according to the glass sample, so that it is near the T_g,

such as near 280°C for $NaPO_3$ and or at the optimum temperature where the glass is not deformed and would not form a solid-block glass.

21. Applicant asserts that Glajch teaches that nitriding phosphate starting glass "produces glasses containing up to 12 wt % nitrogen. As discussed above, Glajch teaches that this process "increases the chemical stability" of the glass. Brow's and Yashchishin's surface nitriding methods produce glasses that incorporate "up to 3-5% and "0.5-2%" nitrogen, respectively, i.e., amounts far lower than that of Glajch. Assuming that one of skill in the art would have substituted Brow's and/or Yashchishin's nitriding methods for Glajch's nitriding method, which they would not, they would have obtained a less stable glass. Accordingly, Applicant submits that one of skill in the art would have no reason to substitute Brow's and/or Yashchishin's inferior nitriding methods for Glajch's nitriding method.

22. First, the reference of Brow teaches that atom% nitrogen is varied between 2 and 6 at% and 2 to 8 at% after various sputtering times, increasing ammonia treatment times, nitriding temperatures, etc. (p174, left column; figure 1). Therefore, it would have been obvious to vary the sputtering time, nitriding temperatures, etc. to alter the % of nitrogen in the nitrogen layer.

23. Glajch et al. teaches of nitriding nitriding phosphate starting glass "produces glasses containing up to 12 wt % nitrogen which does not exclude the up to 3-5% (2-6 at% and 2-8 at%) and "0.5-2%" nitrogen, respectively of Brow and Yashchishin.

24. The instant claims recite, “nitrogen rich surface layer comprises up to about 15 molar % nitrogen” which does not exclude the up to 3-5% (2-6 at% and 2-8 at%) and "0.5-2%" nitrogen, respectively of Brow and Yashchishin.

25. Applicant asserts that Glajch teaches that its nitriding process "is expected to decrease the dissolution rate of the solid in water." Glajch's nitriding method is based on a method disclosed by Reidmeyer et al. (J. Non-Crystalline Solids 1986, 85:186-203, hereinafter "Reidmeyer"). Reidmeyer teaches that the dissolution rate of glass treated with 11.75 % nitrogen (i.e., Reidmeyer/Glajch nitriding method) is 1000 times slower than the dissolution rate of base glass (i.e., glass not treated with nitrogen). Yashchishin and Brow suggest that the dissolution rate of their treated glass is only about 3 to 6 times and 10 times, respectively, slower than the dissolution rate of base glass. As such, one of skill in the art would understand that glass treated using Yashchishin's or Brow's method would dissolve significantly faster than glass made using Glajch's method. Accordingly, there is no reason why one of skill in the art would substitute Glajch's nitriding method, which seeks to decrease the dissolution rate, with a nitriding method that results in a faster dissolution rate than that of Glajch.

26. Brow teaches of the advantages provided by a nitrogen surface layer on the phosphate glass, such as increased aqueous durability, increased chemical durability, etc. wherein the dissolution rates are shown in fig 4 wherein the dissolution rates for the nitrogen surface phosphate glasses approach 6 x 10^{-8} g/cm^{2}min and are up to 20 times better than the base glass (figure 4; p175, left column, first full paragraph).

27. Yashchishin teaches the advantages of improved chemical stability by 3 to 6 times, microhardness and thermal stability are increased by a factor of 1.5 as well as water repellency of the glass surface.

28. Therefore, it would have been obvious and predictable to one ordinarily skilled in the art to provide a nitrogen surface on the phosphate glass of Glajch to provide for the advantages of increased aqueous durability, increased chemical durability, microhardness, etc.

29. Applicant asserts that the claimed implant materials comprise a nitrogen-rich surface layer that assists in, for example, preventing the premature start of bioresorption and the premature release of radioisotopes. Delaying bioresorption and leakage of radioisotopes is advantageous for various radiotherapies such as the treatment of liver cancer. As such, one of skill in the art would understand that, in order for the claimed implant materials to work for their intended purpose, the nitrogen-rich surface layer would necessarily surround the implant materials. Glajch teaches a method of making phosphate glass particles by melting phosphate glass into a "bulk" glass and crushing the phosphate glass into particles. Brow and Yashchishin disclose methods of nitriding "bulk" materials. Assuming one of skill in the art had a reason to apply Brow's and/or Yashchishin's methods to Glajch, which they would not, the skilled artisan would nitride Glajch's bulk glass and then crush the nitrided bulk glass into particles. One of skill in the art would understand that crushing bulk glass into particles will necessarily result in particles that do not have any nitrogen, let alone a nitrogen-rich surface layer (e.g., a particle formed from the middle of the bulk glass would not have any nitrogen on its

surface). Indeed, these particles would not result in the claimed implant materials, nor would they be useful for radiotherapy. Accordingly, even assuming one of skill in the art substituted Brow's and/or Yashchishin's nitriding methods for Glajch's nitriding method, this hypothetical method would not produce the claimed implant materials.

Applicant also submits that one of skill in the art would not have a reason to apply Brow's and/or Yashchishin's methods to Glajch's crushed glass.

30. The references of Brow and Yashchishin disclose methods of nitriding phosphate glasses. At the time of the invention it would have been obvious to one ordinarily skilled in the art that the method of nitriding the phosphate glasses can be applied to particles of smaller sizes, such as particles, powders as nothing in the references exclude nitriding particles, powders of smaller sizes and the methods of Brow and Yashchishin do not deformed in phosphate glass the process and thus the sizes are not altered.

31. The references of Brow and Yashchishin were not used to teach of nitriding bulk glasses and then crushing the nitrided bulk glass into particle but were used to teach of nitriding of phosphate glasses wherein the method of nitriding the phosphate glasses of Brow and Yashchishin can be applied to particles of smaller sizes, such as particles, powders as nothing in the references exclude nitriding particles, powders of smaller sizes and the methods of Brow and Yashchishin do not deformed in phosphate glass the process and thus the sizes are not altered.

32. Also, the nitrogen layer on the surface of the phosphate glass of the combined references of Glajch et al. Brow et al. and/or Yashchishin et al. to improve it’s chemical stability (by 3 to 6 times), mechanical strength, etc. without changing its chemical

composition encompasses the nitrogen rich surface layer of the instant claims and is capable of the same functions and has the same properties, such as substantially preventing premature release of said radioactive isotope or combination of radioisotopes for up to 10 half-lives of the longest lived radioisotope in said implant.

Conclusion

33. No claims are allowed at this time.

34. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA PERREIRA whose telephone number is (571)272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/Melissa Perreira/
Examiner, Art Unit 1618